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Study of various pharmacological action and medicinal values in the leaves, seeds and flowers of Nyctanthes Arbor tristis

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Abstract

Nyctanthes arbor-tristis (NAT) also known as Parijata or Harsinghar is an Indian traditional plant of great importance. It has been used in Ayurveda, Siddha and Unani system of medicine for treatment of various infectious and non-infectious diseases. Each part of the plant has some medicinal value and is used for various pharmacological actions such as anti-arthritic, antispasmodic, antibacterial, anti-inflammatory, immunostimulant, antidiabetic, hepatoprotective, antioxidant, antimicrobial, anthelminthic, antileishmanial, anti-pyretic, anti-allergic, antiviral and CNS depressant. The phytochemical analysis of plant revealed presence of flavonoids, tannins, saponins, glycosides, alkaloids, steroids and phenolic compounds which are responsible for these pharmacological actions of the plant. The chemical drugs being used for treating various ailments are costly and moreover have various side effects. These drugs can be replaced by the herbal plants which have no such side effects and are cost efficient, and one such alternative can be NAT. This paper reviews recent researches, importance, applications, methods of propagation and future prospects of NAT. Particular emphasis has been given towards the applications and methods of propagation of the plant.

Keywords: nyctanthes arbour, tristis, Indian traditional plant, Morphological Characters, medicinal value, side effect, etc

Introduction

Parijat, that goes by the scientific name Nyctanthes arbor tristis belongs to the Oleaceae family. It is a small tree or a shrub growing up to 33 feet tall with a grey flaky bark. The leaves are quite broad, lanceolate with a margin. The flowers look breath-taking with 5 to 8 white corolla petals, having an orangish-red centre. They mainly bloom at night, and fall down as the dawn appears, forming the white icy carpet. The fruit of this plant is brown in colour, round to heart shaped capsule of 2 cm diameter containing a single seed. Parijat chiefly grows on rocky ground in dry hill shades, dry deciduous forests or at sea-level up to 1500 m altitude with a wide range of rainfall patterns, from seasonal to non-seasonal and is tolerant to moderate shade. It thrives well in a wide variety of loamy soils and in soils found in average gardening environments. This flower is found in abundance in West Bengal, India and also in Kanchanaburi Province in Thailand. Parijat is loaded with medicinal qualities and is native to Southeast Asia and South Asia.

Various synthetic drugs are being used as medicine for treatment of diseases that comprise various side effects. Plants are source of various chemical substances that possess immense biological properties which can be used as alternative to these synthetic drugs. Various plants were explored as source of bioactive agents that could treat different ailments. Among 4, 22, 000 flowering plants from the whole world, more than 50,000 plants are there which reportedly have medicinal and pharmacological use [1] . Nyctanthes arbor-tristis Linn. (NAT), a small divine ornamental tree, is used to pray God across India and is known for its fragrant white flowers. The plant is a well-known traditional Indian medicinal plant also, which in Ayurveda is used for various pharmacological actions such as anti-arthritic, antispasmodic, antibacterial, anti-inflammatory, immunostimulant, antidiabetic, hepatoprotective, antioxidant, antimicrobial, anthelminthic, antileishmanial, anti-pyretic, anti-allergic, antiviral and CNS depressant. It is an herbal remedy for treating sciatica, malaria, enlargement of spleen and other various infectious and non-infectious diseases. It is also used as blood purifier. NAT in local language is commonly known as Hardingham, Parijata or night flowering jasmine [2, 3, 4]. The generic name 'Nyctanthes' came from the Greek words 'Nykhta' meaning 'night' and 'anthos' meaning 'flower' while the specific name 'arbortristis' means 'the sad tree' because of the dull look of tree during the daytime [5] . The plant is native to the subtropical Himalayas of Nepal and India and geographically distributed in southern parts of India, northern Pakistan and in south-east Asian countries like Thailand, Malaysia and Indonesia [6]. In India, it is distributed in the outer Himalayas and tract of Jammu and Kashmir, Nepal to East Assam, Bengal, Tripura and extended throughout the central region up to Godavari in south [1] .

Morphological Characters

It is a terrestrial woody shrub with white flowers having an extraordinarily strong and pleasant fragrance whole night that grows up to 10 meters in height and have a life span of 5-20 years [7]. The plant can be cultivated in tropical and subtropical regions all over the world, from sea-level up to 1500m altitude at the equator [6]. It usually grows in red and black soil with pH of 5.6-7.5 and prefers arid and semi-arid climatic conditions [1]. Flowering generally occur from July to October and flowers are arranged at the tip of branches or in axil of the leaves in cluster of 2-7 flowers together, each flower opening at dusk and falling at dawn. These flowers are fragrant and sessile having 6-8mm long, narrowly campanulate, hairy outside, glabrous inside, ciliated calyx and more than 13mm long, 6-8mm long tube, 5-8 unequally obcordate and cuneate lobed white corolla with an orangered centre. Two stamens are inserted near the top of corolla tube and stigma is obscurely bifid. The fruits are flat, compressed, brown heart-shaped to round capsules with two sections each containing a single seed. Seeds are exalbuminous, testa are thick and outer layer of large transparent cells is heavily vascularized while cotyledons are flat, and radicle is inferior. The leaves are rough, hairy, decussately opposite, simple, 6-12 cm long, 2-6.5 cm wide with an entire margin. [8, 9]

a) Nyctanthes arbor-tristis Flowers and Seeds

b) Leaves

c) Fruits

d) Stem

e) Flowers

f) Leaves

Taxonomical Classification

Kingdom: Plantae

Subkingdom: Viridiplantae

Infrakingdom: Streptophyta

Superdivision: Embryophyta

Division: Tracheophyta

Subdivision: Spermatophytina

Order: Lamiales

Family: Oleaceae

Genus: Nyctanthes

Species: Nyctanthes arbor-tristis

Medicinal Usage of Various Parts of NAT

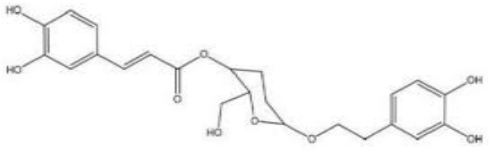
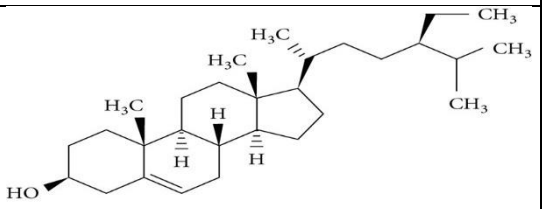
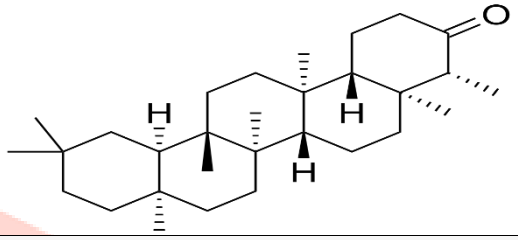
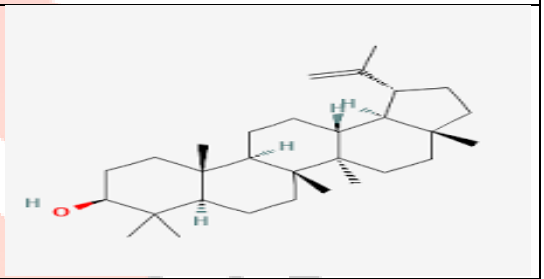
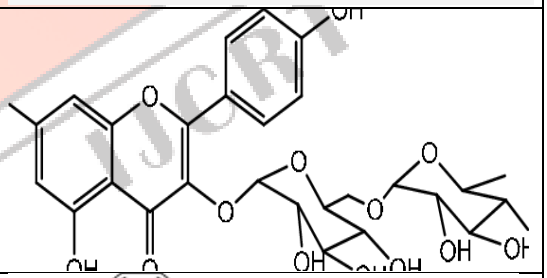
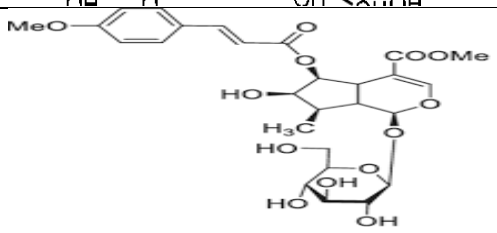
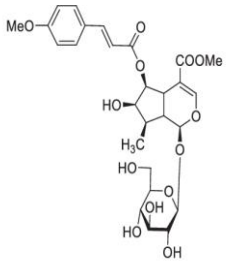
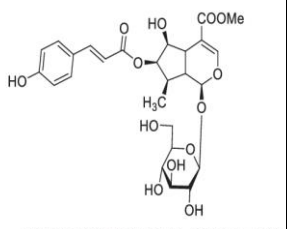
In Ayurveda, Siddha and Unani System Nyctanthe arbor-tristis has been used by tribal people of India (Orissa and Bihar) along with its use in Ayurveda, Siddha and Unani system of medicines for many years. Various pharmacological actions of different parts of plant have been investigated [10]. Seeds are used as anthelminthic, in alopecia, bilious pyrexia and powdered form is used for curing scurfy affections of scalp, piles and skin diseases [3]. Powdered stem bark is given to patients with rheumatic joint pain, used as an expectorant, in treatment of malaria, snakebite, bronchitis, ulcers, bleeding gums, anorexia, liver disorders, piles, worm infestation, blood disorder, oliguria, skin diseases and fever. Stem bark pounded with Zingiber officinale and Piper longum is boiled in water and there sultant liquid is taken for two days for treatment of malaria while the resultant paste on mixing with Arjuna bark is rubbed on the body for treatment of internal injury and joint broken bones. The oil prepared out of the bark of the plant is mixed with rice gruel and rock salt to prepare a dose form (called anjana in ayurveda)

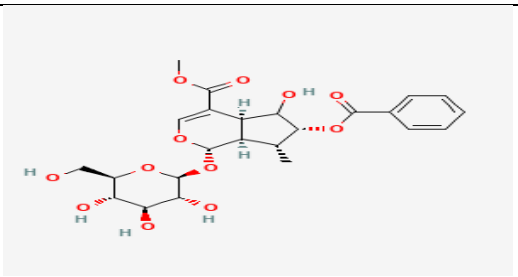
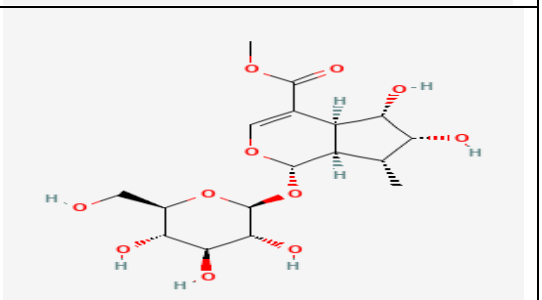
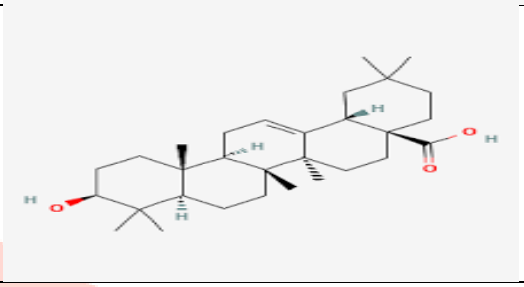
used to apply in sclera of eye is found to be beneficial for various eye diseases [3, 6, 11]. Leaves are used for the treatment of various diseases such as obstinate sciatica, chronic pyrexia, rheumatism, intestinal worm infection, anorexia, haemorrhoid, liver disorders, biliary disorders, pyrexia with rigors, and as laxative, diaphoretic, diuretic and antidote to reptile venom. Leaf succulent mixed in honey, given thrice daily is effective in cough. Paste of leaves with honey is also given for treatment of pyrexia, high blood pressure, diabetes and leaf juice with honey is used to cure chronic fever and with loha- bhasma (mineral based ayurvedic medicine that contains elemental iron micro-fine particles prepared through the process of calcination under high temperature) is used in anaemia and hepato-biliary diseases (hepatic and spleen enlargement) while decoction of leaves is specifically recommended for obstinate sciatica. Bitter extract from leaves is given to children for expulsion of roundworms and threadworms and fresh leaves are used for preparing homeopathic medicines [3, 6, 8]. The juice of 3-7 leaves is used as blood purifier to prevent skin infection by tribal people in Orrisa [10]. Flowers are used as stomachic, carminative, astringent to bowel, anti-bilious, expectorant, hair tonic and treatment of haemorrhoid, obstinate remittent fever, sciatica, rheumatism, various skin diseases and for ophthalmic purposes [3, 6]. Decoction of flowers given orally to ward off wind in stomach, stimulate gastric secretion, improves expectoration of lungs and used in treatment of gout [12]. Roots are used for emaciation [4].

Chemical Constituents of NAT

A variety of chemical constituent belonging to different classes such as terpenes, steroids, glycosides, flavonoids, alkaloids and aliphatic compounds were isolated and identified in various parts of NAT. Glycosides and alkaloids, the secondary metabolites, are the largest group of chemicals produced by the plant. Glycoside and two alkaloids, one soluble in water and other in chloroform, was isolated from the bark. Roots are found to be composed of alkaloids, tannins and glucosides while leaves contain tannic acid, methyl salicylate, mannitol, β-sitosterol, flavanol glycosides, Astringent, Sugar, an amorphous glycoside 1%, mannitol 3%, amorphous resins 1.2%, ascorbic acid, oleanolic acid, nyctanthic acid, benzoic acid, Friedelin, lupeol, carotene and traces of volatile oil. It was found that frying the leaves in oil increases ascorbic acid content. Iridoid glycosides and arbortristoside A, B, D and E is found in seeds. Seed kernel yields 12-16% of pale-yellow brown fixed oil that contains glucosides of linoleic, oleic, lignoceric, stearic, palmitic acid, 3,4-secotriterpene acid and β-sitosterozl. Flowers consist of essential oil, nyctanthin, D- mannitol, tannin, glucose, carotenoids, glycosides, β- monogentiobioside ester of α-crocetin (or crocetin-3), β- monogentiobioside, β-D monoglucoside ester of α-crocetin, β-digentiobioside ester of α-crocetin (or crocin-1). Phytochemical analysis of ethanolic extract of flower revealed presence of rengyolone, a cyclohexylethanoid, iridoid glycosides (6-o-trans-cinnamoyl-7-o-acetyl-6β- hydroxyloganin, arborside C, 6β-hydroxyloganin) and a phenylpropanoid glycoside, nyctanthoside. [8, 13, 14]. Flower oil consists of α-pinen, p-cymene, 1-hexanol, methylheptanone, phenyl acetaldehyde, 1-decanol and anisaldehyde [15]. Bright orange corolla tubes of flower contain a colouring substance nyctanthin which is identical to α-crocetin ($C_{20}H_{24}O_4$) from saffron. The corolla tubes were formerly used for dyeing silk, sometimes together with safflower or turmeric [3].

Some Phytoconstituents of Nat, Their Class and Structure

Sr. No.	Phytoconstituent	Chemical Class	Parts of plant constituting the phytochemical	Structure of the phytoconstituent
1.	Desrhamnosylverbacoside	Iridoid Glycoside	Leaf	
2.	β-sitosterol	Steroid	Leaf, stem, seed	 β-Sitosterol
3.	Friedeline	Terpenes	Leaf	
4.	Lupeol	Terpenes	Leaf	
5.	Nicotiflorin	Flavonoid	Leaf	
6.	Arbortristoside A, B, C, D and E	Iridoid Glycoside	Seed	 Arbortristoside A
7.	6-o-trans-cinnamoyl-7-o-acetyl-6β-hydroxyloganin	Iridoid Glycoside	Flower	 Arbortristoside - A  7-O-trans-cinnamoyl- 6 beta- hydroxyloganin

8.	Arborside C	Iridoid Glycoside	Flower	
9.	6β-hydroxyloganin	Iridoid Glycoside	Flower	
10.	Oleanolic acid	Terpenes	Leaf	

Pharmacological Applications of NAT

Hypoglycemic and hypolipidemic activity:

Diabetes mellitus is a major global disease from which millions of people are suffering. In diabetes, it is important not only to control blood glucose level but also the blood lipid level as diabetes tends to increase low-density lipoprotein cholesterol and decrease high-density lipoprotein cholesterol levels in blood that triggers coronary occlusions and blocks. It has been concluded that the present treatment of diabetes using synthetic hypoglycaemic agents may cause adverse effects resulting in hypoglycaemia, gastro-intestinal disturbances, renal toxicity and hepatotoxicity and this is why plants are been considered as an alternative. Different doses of boiled aqueous extract of fresh NAT flowers were examined for the hypoglycaemic and hypolipidemic activity in mice. 200, 500 and 750mg/kg of the extract was administered in mice and subsequently fasting and random glucose concentration were examined. After oral administration of the extract, the effect of extract on glucose tolerance, gastrointestinal glucose absorption, liver and skeletal muscle glycogen content, diaphragm uptake, serum lipid profile and in-vitro amylase assay were examined in mice. The experimental results concluded that 500 and 750 mg/kg of the extract reduced fasting glucose levels by 49% and 39% respectively at 4hr post-treatment while 500 mg/kg of the extract decreased the random blood glucose level significantly by 32% at 4hr post treatment. The extract also significantly inhibited glucose absorption from intestine by 85%, increased diaphragm uptake of glucose by 64%, decreased level of total cholesterol and triglycerides by 44.8% and 53% respectively, and increased the high-density lipoprotein cholesterol by 57%. It also exhibits inhibition of α-amylase enzyme activity by 16.66%. The biochemical and toxicological effect of the extract neither showed any deaths nor there were any signs of clinical toxicity, stress and aversive behaviour during treatment period. Further histopathology analysis of liver and kidney portion after treatment with extract did not show any effect. The experimental data concluded that the boiled aqueous extract of fresh NAT flowers possess hypoglycaemic and hypolipidemic activity which can be used as an alternative medicine for treatment of diabetes and toxicological results considered it safe for oral administration [24].

Antibacterial activity:

Antibacterial activity of flower, leaf, seed and fruit ethyl acetate and chloroform extract against gram-positive (Staphylococcus aureus) and gram- negative (E. coli, Klebsiella pneumoniae, Pseudomonas aeruginosa) bacteria was examined by K. Priya et al, 2007. 300 µl of both ethyl acetate and chloroform extract showed significant antibacterial activity against the bacteria tested. Flower ethyl acetate and seed chloroform extract showed broad spectrum antibacterial activity against gram-negative as well as gram-positive bacteria while leaf extract showed antibacterial activity against only but all the gram-negative bacteria. Fruit and seed ethyl acetate while flower and seed chloroform extract showed inhibitory effect against only Pseudomonas aeruginosa and Klebsiella pneumoniae. It was also found that the antibacterial activity of fresh plant parts was more than that of the dried one. Phytochemical analysis revealed presence of phytosterols, phenolics, tannins, flavonoids, glycosides and saponins. Phenolic compounds and tannin were found to be active against the bacteria. Tannins have been found to form irreversible complexes with proline rich proteins that results in inhibition of the cell protein synthesis and play an important role as stable and potent antioxidant, astringent and in treatment of diarrhoea and dysentery [4].

Anti-fungal activity:

Different parts of NAT plant were examined for antifungal activity against three most prevalent clinical pathogenic fungi- Aspergillus niger, Penicillium and Aspergillus flavus. Fresh and mature leaves, seeds, stem, bark and flowers were collected and dried, and extraction was performed with distilled water, methanol and chloroform. The antifungal activity of the extracts was measured by well diffusion method in terms of "zone of inhibition" of fungal growth. The results revealed that only distilled water extract of stem and bark of NAT showed antifungal activity against A. niger only while chloroform extract of leaves was only effective against A. flavus. The study showed that the most effective results for antifungal activity was shown by methanolic extract of leaves, stem and bark of NAT against both Aspergillus and Penicillium [5].

Anti-viral activity:

Anti-viral activity of NAT was examined against encephalomyocarditis (EMCV) and Semliki Forest Viruses (SFV) in Swiss albino mice. The experimental results showed that the crude ethanolic extract, n-butanol fraction and isolated iridoid glycosides (Arbortristosides A and C) showed inhibition of 75% of cytopathic effect caused by both the viruses. In-vivo studies against EMCV at different doses showed that the crude ethanolic extract and n-butanol fraction protected 40% of animals infected with EMCV at 250mg/kg body weight dose while the aqueous fraction protected 50% of animals infected with EMCV at 125 mg/kg body weight dose. Whereas in case of in-vivo anti-SFV activity the result was most promising with n-butanol fraction that provided 60% protection to animals infected with SFV at 125 and 62.5 mg/kg body weight dose and Arbortristoside A that also protected 60% of SFV infected animals but at a much lower dose of 31.2mg/kg body weight. Both these fractions and isolated compounds did not produce any significant antiviral activity when administered orally. Further study revealed that with increasing dose of virus (SFV) the level of protection declined. However, animal treated with Arbortristoside A recorded 66, 65 and 50% protection against 5, 10 and 100 LD50 concentration. Based on the experimental results, it was concluded that the arbortristiside A isolated from n-butanol fraction of NAT possess maximum antiviral activity against enveloped virus (SFV) while moderate antiviral activity of n-butanol fraction was observed against EMCV. It was also observed that the antiviral activity of n-butanol and arbortristiside A and C depends upon the route of administration, challenged virus concentration and dose of the compound [23].

Antioxidant activity:

Anowar et al in their work on the plant concluded the oxidative and protective role of hydro- alcoholic flower extract of NAT against the oxidative stress of hydrogen peroxide, H_2O_2. H_2O_2 is weak oxidising agent that can penetrate the cell membrane and enter the cell where it reacts with Fe^{2+} and Cu^{2+} ions and forms hydroxyl radicals. These hydroxyl radicals further cause damage to the cell by interacting with the micro and macromolecules in the cell and inactivate enzymes usually by oxidation of the thiol (-SH) groups. They treated the lymphocytes isolated from chicken blood with H_2O_2 that decreased the viability of cells by lowering the cellular antioxidant, reduced glutathione (GSH). The level of GSH was increased by 1.22-fold significantly when the lymphocytes were treated with the flower extract of NAT. At the same time, the specific activity of marker of membrane damage, lactate dehydrogenase (LDH) was also found to decrease as compared to intreated lymphocytes that suggests the non-toxic effect of extract on the cellular system. The experimental data of the

study showed the antioxidant property of the crude extract of NAT [2]. Some other research has concluded leaves and stem of Nyctanthes arbor-tristis as a potential source of natural antioxidant. Phytochemical analysis of stem and leaves of the plant showed presence of flavonoids, tannins, saponins, glycosides, alkaloids, steroids and phenolic compounds. The antioxidant activity of NAT might be considered due to the phenolic compounds which act as free radical terminators [8].

Analgesic and anti-inflammatory activity:

The pathophysiological response of mammalian tissue towards various hostile agents such as infectious organisms, toxic chemicals, physical injury or tumor growth is called inflammation. Edema formation, leukocytes infiltration and granuloma formation are components of inflammation. Glucocorticosteroids and nonsteroidal anti-inflammatory drugs (NSAIDs) are the two main types of anti-inflammatory agents but due to their adverse side effects various alternatives of NSAIDs and opiates are being searched all over the world. NAT was examined for the same and experiments were carried out on various animal models. The methanolic extract of NAT stem bark showed the analgesic and anti-inflammatory activity by preventing stimulation of nociceptive components which may happened due the inhibition of the production of prostaglandin and related compounds. Experimental results also showed that the extract reduced the rate of edema in carrageenan- induced rat paw edema model [21]. The peripheral analgesic activity of leaf extract of NAT was studied in mice using the acetic acid induced writhing test. Studies revealed that the presence of flavonoids in NAT might be responsible for the analgesic activity of the plant. Flavonoids are known for inhibiting synthesis of prostaglandin which are involved in pain perception by inhibiting cyclooxygenase enzyme. Other chemicals like methyl salicylate and benzoic acid which have strong analgesic effect are also found in NAT [22].

Anti-pyretic activity:

Fever is a complex physiological response which is triggered by infectious or aseptic stimuli that results in elevated body temperature which occur due to increase in concentration of prostaglandin E (2) in certain parts of brain that further alter the firing rate of neurons that control thermoregulation in hypothalamus [30]. Antipyretics are drugs that reduce the elevated body temperature. NAT was examined for antipyretic activity in albino rats for potential on normal body temperature and yeast-induced pyrexia. The whole plant extract of NAT showed significant antipyretic activity at the dose of 200 mg/kg by reducing normal body temperature and yeast-provoked elevated temperature in dose dependent manner. It was also found that the effect of whole plant extract of NAT dose was comparable to that of paracetamol (150 mg/kg), a standard antipyretic agent [31]. In another study the petroleum ether and methanol extracts of NAT bark were examined for the antipyretic activity of the plant against yeast induced pyrexia in mice. Fever was induced by 20% aqueous solution (10 mg/kg) of Brewer's yeast subcutaneously injected into the dorsum region of mice and aspirin (150 mg/kg) was used as standard drug. It was found that both petroleum ether and methanol extract (100 mg/kg and 200 mg/kg) showed antipyretic activity by significantly reducing rectal temperature after its administration [29].

Anti-cancer activity:

The methanolic crude extract of leaf, fruit and stem of NAT were examined in-vitro for antioxidant and anticancer activity of plant. By DPPH free radical scavenging assay antioxidant activity of extract was evaluated, it was reported that the dried fruit methanol extract of NAT showed 93.8% scavenging effect of phenolic crude at 1000 mg/ml conc., dried stem methanolic extract showed a moderate value of 69.9% at 100 mg/ml conc. while least value was 27.8% that was observed with dried leaves methanol extract at 1.0 mg/ml conc. Based on antioxidant activities the anti-cancer activity was evaluated by MTT assay on MDB MB-231 cancer cell lines. It was found that out of all the extracts, dried fruit methanol extract showed high degree of inhibition against human breast cancer cell lines (MDA-MB 231). The phytochemicals isolated from NAT dried fruit methanol extract were glycosides, tannins, phenols and steroids which were predicted to be responsible for the anticancer activity of the plant [34]. In another study, the methanolic extract of leaves of NAT were examined for anti-cancer activity of the plant against Ehrlich Ascites Carcinoma (EAC) cells (107 cells/mouse) where the extract was injected into intraperitoneal route (200 and 400 mg/kg body weight) of Swiss Albino mice. For the study 5-Fluorouracil (20mg/kg body weight) was injected through intraperitoneal route as standard anti-cancer drug. Based on the ability to inhibit cancer cell growth in ascitic fluid of mice, the anticancer activity of the extract was evaluated. Various parameters were taken to establish the potency of the anticancer property of methanol extract of NAT

leaves including percentage inhibition of total cell count, tumour volume, viable and non-viable cell counts; percentage increase in life span and hematological parameters. Administration of extract at the doses of 200 and 400mg/kg b.w. significantly reduced the total cell count and tumour volume. At 200 mg/kg conc. the percentage of inhibition of total cell count and percentage inhibition of tumour volume was observed to be 84.75% and 75.52% respectively while at 400 mg/kg conc. the percentage of inhibition of total cell count and percentage inhibition of tumour volume was observed to be 90.36% and 96.37% respectively. Administration of extract at doses of 200 and 400 mg/kg also significantly decreased the viable cell count and level of WBC while increased non-viable cell count, life span and the level of both RBC and haemoglobin. The overall results of the study concluded that the methanol extract of NAT leaves possess anticancer activity [28]

Wound healing activity:

The wound healing activity of NAT was tested on Wistar albino rats by Matadeen et al, 2011.The rats were treated with 2% w/w NAT methanolic extract for 16 days. It was found that the complete epithelization of both incision and excision wounds took about 16 days and wounds were completely healed. It was concluded that 300mg dose/kg of NAT extract can be considered a good solution for healing both the types of wounds [19].

Hepatoprotective activity:

Petroleum ether and methanol extract of NAT bark were examined for the hepatoprotective activity using carbon tetrachloride (CCl4) induced hepatotoxicity in Swiss albino mice. The hepatic toxicity was induced in the liver of mice by injecting CCl4 and the level of Serum Glutamate Pyruvic Transaminase (SGPT), Serum Glutamate Oxaloacetic Transaminase (SGOT), Alkaline phosphate (ALP), Direct Bilirubin (DB) and Total Bilirubin (TB) in the serum of mice was measured for determining the function of liver. Silymarin was used as standard drug for the study. The administration of Silymarin and both the extracts (100 mg/kg and 200 mg/kg) significantly decreased the serum marker enzymes (SGPT, SGOT, ALP, DB & TB). The dose of 200 mg/kg of methanol extract was found to be more effective in comparison to that of 100mg/kg methanol and 100 mg/kg and 200 mg/kg of petroleum ether extract of NAT. The phytochemical analysis of petroleum ether and methanol extract of NAT showed presence of alkaloid, cardiac glycosides, tannin, saponin, terpenoid, phlobatannins, fixed oils, fats and flavonoids that might be responsible for the activity [29].

CNS depressant action:

A study was carried out with water soluble portion of ethanol extracts of flowers, barks, seed and leaves of NAT to evaluate CNS depressant activity of plant. It has been already concluded that the leaves of the plant possess hypnotic and tranquilizing activity whereas its flower possess sedative activity. The ethanol extract of plant was extracted by Soxhlet extraction and the extract was examined for the pharmacological activity in adult male Swiss mice. The CNS depressant activity was evaluated by observing the prolongation of sleeping in mice induced by pentobarbital sodium. The attempts were made to determine the possible mechanism behind the activity by determining their effect on brain monoamine neurotransmitters like serotonin and dopamine. The study showed that the ethanolic extract of leaves, flowers, seeds and bark (600 mg/kg) of NAT possess significant CNS depressant activity and some muscle relaxant activity. The leaves, flowers, seeds and bark showed significant and dose dependent prolongation of the onset and duration of sleep, which was comparable to chlorpromazine, the standard drug. The highest CNS depressant activity was observed to be possessed by the leaves. It was also concluded that the activity possess by the extract might be due to the decrease in dopamine and increase in serotonin level in brain [28].

Anti-spasmodic activity:

A study taken on NAT for antispasmodic activity of the plant was estimated using guinea pig ileum preparation against acetylcholine, a spasmodic agent. Antispasmodic activity of ethanolic extract of different parts of plant was estimated on the basis of inhibition of contractile effect of acetyl choline by various dilution of the extract, out of which flower and seed extract were the most effective. The contractile response of 0.0002mg of acetylcholine was inhibited by 72mg of flower and 90mg of seed extract which was less than that of 16mg piperazine citrate [27].

Antihyperlipidemic activity:

Hyperlipidaemia is increased level of lipid in blood which is first and for most factor responsible for diseases like atherosclerosis, coronary heart disease, ischemic cerebro-vascular disease, hypertension, obesity and diabetes mellitus (Type II) etc. Methanolic extract of NAT leaves was examined for antihyperlipidemic activity in Wistar albino rats. The extract at the doses of 200 and 400 mg/kg body weight showed significant decrease in lipid profile like triglycerides, total cholesterol (TC), low density lipoprotein (LDL), very low-density lipoprotein (VLDL), and significant increase in high density lipoprotein (HDL). The effect of lipid lowering might be result of plant sterols (β-stigmasterol and β-sitosterol) which reduce cholesterol absorption and thus increase faecal excretion of steroids and thus results in decrease of body lipids. It was concluded that the methanolic extract of NAT leaves showed antihyperlipidemic activity with specific and non-specific mechanism which might be due to the presence of phytochemicals like phenol, triterpenoids and flavonoids in the extract [25].

Antihistaminic and Anti-asthmatic activity:

Catalepsy is a condition where the limbs remain in whatever position they are placed. It is characterized by lack of response to the external stimuli and muscle rigidity and can be induced by neuroleptic drugs [16]. Experimental results proved that the clonidine-induced catalepsy can be inhibited by the petroleum ether extract of NAT bark. The effect of clonidine-induced catalepsy in Albino mice was studied and it was concluded that the cataleptic effect of clonidine in mouse is mediated by histamine from the mast cell and due to the mast cell stabilizing property of the NAT, this extract was able to inhibit the clonidine-induced catalepsy. The observation of this study indicated the antihistaminic activity of NAT bark and concluded that it may be useful in treatment of asthma [17]. Allergic asthma is a chronic inflammatory disease that affects breathing. It is characterized by bronchial obstruction reactions, airway inflammation and airway hyper-reactivity towards variety of stimuli like allergens, histamine, methacholine, etc. When exposed to allergen, the main component of the early asthmatic reaction is bronchoconstriction and it was concluded that under asthmatic conditions, the bronchial obstruction reaction and airway hyper-sensitivity are associated with the deficiency of nitric oxide production which plays a major role in maintenance of airway balance. The ethanolic extract of NAT leaves were examined for histamine-induced dose-dependent contraction of tracheal smooth muscles which concluded that the extract could inhibit the contractile responses produced by histamine and thus confirmed the bronchodilatory activity of the ethanolic extract of NAT leaves on airway smooth muscles. The results of experiment showed that the acting mechanism of the extract is through increase in production of nitrogen oxide, NO. It has also been concluded that the anti-asthmatic and anti-allergic activity of NAT leaves is due to the presence of β-sitosterol [18].

Method of Propagation

Due to its peculiar and pleasant fragrance it is often cultivated in garden. The shrubs can be propagated by seeds as well as by cutting, but the phenolic compounds leaching out of the imbibed seed decreases the rate of germination by seeds [12]. Due to low seed setting, poor germination by seed because of the inhibitory compounds and attack of insects during ripening stage, many young seedlings die under natural conditions and thus propagation of NAT by seed becomes very difficult [33, 31]. The inhibitory phenolic compounds are stored in the pericarp of the seed coat. It was studied that by either removing both the coverings or treating seeds with a solution of antioxidants like polyvinylpyrrolidine (PVP) and polyvinylpolypyrrolidine (PVPP) prior to germination can improve germination rate [12]. In the Red Data Book, NAT has been recorded as a 'valuable plant' which is critically endangered and at extremely high risk of extinction in the wild. Therefore, it is highlighted for conservation in many documentations for which in-vitro propagation is been used. The natural propagation of NAT is also a slow process that could not fulfil market demand [31]. The plant is being markedly diminishing due to destruction of its natural environment, excessive over exploitation and unresolved problem of seed viability and poor germination [32]. Hence, for commercial, ornamental and conservation purposes studies are needed to be conducted on production of the plant in large scale [31]. For saving this species from extinction, it is required to propagate these plants using alternative approaches like tissue culture techniques [39]. Plantlets of NAT can be raised by in vitro methods using excised cotyledons, hypocotyls, roots, leaves and bases of internodes that are able readily form callus in the culture. However, calli from cotyledons, hypocotyls and roots exhibited faster growth as compared to those from leaves and internodal bases when cultured in Murashige and Skoog's (MS) media with 2, 4 dichlorophenoxyacetic acid (2,4D), Naphthalene acetic acid (NAA) and coconut milk [12].

Conclusion and Future Prospect

Various synthetic chemicals are being widely used for treatment of different diseases but encompass adverse side effects. Due to these side effects of the drugs, various alternatives are being explored by the researchers and for

the same plants are being studied. One such plant is Nyctanthes arbor-tristis (NAT). The broad-spectrum medicinal use of NAT is the matter of interest for the researchers. The anti-arthritic, antispasmodic, antibacterial, anti-inflammatory, immunostimulant, antidiabetic, hepatoprotective, antioxidant, antimicrobial, anthelminthic, antileishmanial, anti-pyretic, anti-allergic, antiviral and CNS depressant activities of the plant show its great value in the field of medicine. Considering NAT for treatment of various ailments can provide effective and efficient alternative against chemical drugs, which have no side effects and are cost-effective. Further attention and research are required for identification and characterisation of bioactive compound(s) responsible for the biological activity of plant and the elucidation of the mechanism of action in many cases. The toxicity of the various extracts should be considered, as human studies for safety and efficacy of the extracts for long term administration are needed to be proved. Use of various parts of NAT plants in Ayurveda, Siddha and Unani system of medicine should be considered, explored and effective treatment should be elucidated. Tissue culture, recombinant DNA technology and molecular marker-based approaches can be undertaken for increasing production, selection of desired traits of the plant and for studying diversity in germplasm of the species. Other chemical compounds like putrescine should be identified that would help in increasing productivity. Combinational effect of various herbal plants along with NAT can be examined which could provide best alternatives for various ailments as was examined in case of wound healing activity of ethanolic extract of Nyctanthes arbortristis and Murraya koenigii by Jadhav et al, 2017. High potential of plant in management of various ailments, easy availability and requirement of no special condition for its collection and cultivation make it a plant of clinical interest which requires more attention and clinical trials for manufacturing therapeutic preparations that can treat human ailments.

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